Sandra McConkey

History, physical examination

A 4-month-old, female Labrador retriever was presented for steadily worsening altered mentation and drooling, which had begun following her 12th-week vaccination. Occasional head pressing and polydipsia were also seen. The dog was smaller than her littermates and had vomited intermittently between 4 and 7 wk of age.

On physical examination, the puppy was small in stature for her age. Excessive salivation, depression, and irritability were noted. Cranial nerve evaluation was normal.

Laboratory data

Data available for evaluation included a complete blood (cell) count (CBC), a serum biochemical profile, and a urinalysis. These can be found in Table 1.

Important features of the laboratory data

1. Mild, microcytic, normochromic, nonregenerative anemia with large numbers of target cells, and occasional erythrocyte fragments.
2. Mildly elevated serum phosphorous concentration.
3. Markedly decreased serum urea concentration.
4. Mildly elevated serum alkaline phosphatase (ALP) enzyme activity.
5. Moderate panhypoproteinemia.
6. Markedly increased plasma ammonia concentration.
7. Markedly increased pre- and postfasting bile acid concentrations.
8. Presence of ammonium biurate crystals.

Diagnosis

The CBC and serum changes supported decreased hepatic functional capacity, with a portosystemic shunt (PSS) or a hepatic microvascular abnormality being the most likely "rule out." Ultrasonic evaluation confirmed a portosystemic shunt. Ultrasonographic changes included microhepatica, bilateral renomegaly, cystic calculi, and an anomalous portal vessel from the portal vein to the area of the vena cava. Scintigraphic findings showed a shunt fraction of 81.9%.

Discussion

Portosystemic shunts are vascular communications between the portal and systemic venous systems that prevent the normal passage of portal blood through the liver. Clinical signs are variable, often subtle, and typically wax and wane. The most common presenting complaints are nervous signs, such as anorexia, depression, lethargy, ataxia, head-pressing, disorientation, and pacing, and behavioral changes. Hypersalivation, as was seen in this dog, is a common clinical sign in cats with PSS but is very uncommon in dogs (1,2). Intermittent vomiting, diarrhea, and anorexia may be present, and polyuria is common. If urate urolithiasis is present, there may be a history of pollakiuria, dysuria, and hematuria. On physical examination, the animal usually appears normal, although it may show stunted growth. In cats, irises may be gold- or copper-colored.

The nonregenerative, microcytic anemia with target cells and erythrocyte fragments seen in this dog was supportive of a PSS. The CBC in animals with PSS is frequently normal, but a mild nonregenerative anemia can occur. In young dogs, this finding may be difficult to interpret, as puppies typically have lower hematocrits, hemoglobin concentrations, and red blood cell counts than do adults. Microcytosis occurs in 33% to 72% of dogs with a PSS (3), but it can also be associated with iron deficiency (4). The exact mechanism of the microcytosis in this disease is unknown but may be either a functional deficiency or a transport abnormality of iron (3,5–7). Hypochromasia, another hallmark of iron deficiency, occurs in 4% to 100% of animals with a PSS (3). Both PSS and iron deficiency are associated with increased numbers of red cell fragments (schistocytes), as microcytic erythrocytes are less deformable (8). Target cells and poikilocytosis are seen in some dogs with PSS (4). Target cells can be large cells with a higher membrane surface area (leptocytes), such as polychromatophils, which are associated with regeneration, or they may be seen in liver disease, likely due to an abnormality in cholesterol metabolism.

Many of the changes present on the serum biochemical profile were nonspecific. An elevated serum phosphorous concentration is common in young animals, due to bone remodeling associated with growth. An age-related low serum urea concentration is also common, due to a high glomerular filtration rate and anabolic state of growth, but a decreased urea concentration can also be associated with hepatic insufficiency or a low protein diet. In this case, the serum urea concentration was assessed subjectively to be lower than usual for a young animal. However, in many animals with PSS, the urea concentration is normal or only mildly decreased. The low total protein concentration in this dog was due to low globulin and albumin concentrations. The hypoalbuminemia indicated decreased production by the liver or increased loss via the kidneys, intestines, into a third space, or hemorrhage. Hypoglobulinemia can

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Table 1. Laboratory results

Complete blood cell count	Patient value	Reference range
RBC	6.84×10^{12}/L	$5.5–8.5 \times 10^{12}$/L
Hct	0.334 L/L	0.37–0.55 L/L
MCV	48.8 fL	60–77 fL
Retic	34.2×10^{9}/L	$< 127 \times 10^{9}$/L
WBC	12.6×10^{9}/L	$6.0–17.1 \times 10^{9}$/L
Neutrophils	7.686×10^{9}/L	$3.6–11.5 \times 10^{9}$/L
Eosinophils	1.26×10^{9}/L	$0.01–1.25 \times 10^{9}$/L
Lymphocytes	2.14×10^{9}/L	$1.0–4.8 \times 10^{9}$/L
Monocytes	1.512×10^{9}/L	$0.15–1.35 \times 10^{9}$/L
Platelets	Normal	$200–900 \times 10^{9}$/L
2+ Anisocytosis		
4+ Microcytosis		
4+ Target cells		
Occasional RBC fragments		

RBC — red blood cells
Hct — hematocrit
MCV — mean corpuscular volume
Retic — reticulocytes
WBC — white blood cells

Serum biochemical profile	Patient value	Reference range
Sodium	143 mmol/L	144–162 mmol/L
Potassium	4.1 mmol/L	3.6–6.0 mmol/L
Chloride	109 mmol/L	106–126 mmol/L
Calcium	2.39 mmol/L	2.24–3.04 mmol/L
Phosphorous	2.53 mmol/L	0.82–1.87 mmol/L
Urea	0.7 mmol/L	3.0–10.5 mmol/L
Creatinine	51 µmol/L	33–113 µmol/L
Glucose	5.7 mmol/L	3.3–5.6 mmol/L
Cholesterol	7.31 mmol/L	2.50–7.00 mmol/L
Total bilirubin	3 µmol/L	0–17 µmol/L
Alkaline phosphatase	286 U/L	23–87 U/L
Creatine kinase	288 U/L	0–300 U/L
Asparate aminotransferase	50 U/L	20–50 U/L
Alanine aminotransferase	38 U/L	5–69 U/L
Gamma glutamyl transferase	7 U/L	0–8 U/L
Total Protein	36 g/L	51–72 g/L
Albumin	17 g/L	22–38 g/L
Globulin	19 g/L	27–44 g/L
A:G ratio	0.89	0.6–1.5
Lipase	90 U/L	30–560 U/L
SDH	5 U/L	2–20 U/L

A:G — albumin: globulin
SDH — sorbitol dehydrogenase

Special tests		
Ammonium	424 µmol/L	10–82 µmol/L
Bile acids		
Fasting	68 µmol/L	< 10 µmol/L
2 hours post prandial	242 µmol/L	< 20 µmol/L

Urinalysis:
Yellow, cloudy, pH = 8.5
Specific gravity: 1.020
On strip: Negative for protein, glucose, bile, blood, ketones
Urobilinogen 1.7 µmol/L
Microscopic:
1–2 leukocytes/400× field
1–2 transitional cells/400× field
1+ ammonium biurate crystals

also be associated with decreased production by the liver or excessive loss. In this case, however, it was likely age related.

Serum biochemical profiles in animals with PSS can appear normal or have very subtle changes. A decrease in cholesterol, urea, and/or protein (including globulins and albumin) concentration due to decreased hepatic functional capacity is common (1,3). Hypoglycemia can occur in some dogs, especially toy breeds, such as Yorkshire terriers (1). One study has shown that extrahepatic shunts are more likely to be associated with hypoglycemia than are intrahepatic shunts (22% versus 5%) (9). Hypoglycemia is believed to occur due to decreased glycogen storage, decreased insulin catabolism, or endotoxemia (1,9)).

The total bilirubin concentration is usually normal in animals with PSS. If it is elevated, another hepatic disease or interference from hemolysis should be suspected. Serum hepatic enzyme activities may be mildly elevated. Alkaline phosphatase activity increases 2- to 3-fold in 75% of dogs with PSS (9). However, in young dogs, such as this one, it is difficult to assess the importance of the change, as the bone isoenzyme of ALP is expected to cause an age-related increase in total serum ALP activity. As there is minimal hepatocellular cellular injury to allow release of cytosolic enzymes in PSS, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) may be normal or increased by a minimal 2- to 3-fold.

A combination of fasting and postprandial serum bile acid concentrations is one of the best diagnostic tools for detecting decreased hepatic functional capacity and should be done if the history, CBC, or biochemical profile suggests a PSS. Bile acids are initially produced in the liver and are excreted in the bile to aid in the digestion of fats. They are then reabsorbed from the intestine into the portal blood, which transports them to the liver, where the vast majority are removed on the first pass for recycling.

The serum bile acid concentrations in this dog were markedly increased, which indicated a decreased functional capacity of the liver. Preprandial serum bile acid concentration in animals with PSS may be normal to increased (10). The 2-hour postprandial serum bile acid concentrations tend to be markedly increased, often to > 100 µmol/L. Elevated serum bile acid concentrations do not determine a specific etiology. However, certain patterns, such as increased bile acid concentration with no icterus and normal serum enzymes, suggest occult liver disease, such as PSS or cirrhosis (10). Serum bile acid concentrations are more sensitive than are serum hepatic enzyme elevations in detecting PSS (10).

The plasma ammonia concentration was markedly elevated in this dog, also supporting a decreased hepatic functional capacity. Ammonia concentrations are rarely determined anymore, as ammonia is far more labile than are bile acids and can be measured only if a laboratory is nearby. There is also the potential for serious side effects, such as seizures, following administration of ammonium chloride when performing an ammonia tolerance test.

Urine is often isosthenuric in patients with PSS, as was seen here. Ammonium biurate crystals may also be present due to the increased secretion of ammonium and uric acid, which the liver is unable to process normally. Calculi may or may not be present and are not radio-opaque, unless there is a significant amount of phosphate or magnesium present. If calculi are present, there may increased numbers of erythrocytes and leukocytes in the urine.

Follow-up

This dog was placed on a low protein diet (u/d, Hills Pet Nutrition Canada, Mississauga, Ontario), neomycin (Biosol Liquid, The Upjohn Company-Animal Heath Division, Orangeville, Ontario), and a lactulose syrup (PMS-lactulose, Pharmascience, Montreal, Quebec) for the 2-week period prior to surgery. All clinical signs disappeared with medical treatment. At surgery, an extrahepatic vessel was first partially and then fully ligated. Since that time, the dog has done extremely well on a low protein diet.

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BOOK REVIEW

COMPTE RENDU DE LIVRE

Waters M, Voyce M, Zwart P, Frye F. ***A Guide to Lizards CD-ROM.*** Royal Veterinary College, London. 1999. US $55.00.

With the increasing popularity of reptiles as pets, 2 contrasting publications on reptile medicine are timely. A Guide to the Lizards CD-ROM is the first in the Exotics series of tutorial CD-ROMs from the Royal Veterinary College (RVC), University of London. The cover notes state that it is intended to provide veterinarians and their employees with a comprehensive guide to the care and treatment of lizards. It is written by staff of the RVC and 2 of the world's best-known authors on reptiles, with contributions from other leading experts.

The CD-ROM gives practical advice on the medical care of lizards through the use of text, graphics, photographs, video, and interactive case challenges. The program is divided into 4 chapters: Basics, Procedures, Diseases, and Resources. The chapters are subdivided into sections under specific headings. A click on each heading takes you down defined pathways and returns you to the starting menu when the exercise is completed, with a short summary of what you should have learned before you leave. Basics includes biology and husbandry; Procedures is split into examination, theater, diagnostics, and therapy. Despite its billing, this CD-ROM is by no means a comprehensive publication. Diseases covers just 4 conditions: metabolic bone disease, cystic calculi, renal disease, and dystocia, which are all important but do not represent the only diseases encountered in lizard medicine. Other conditions are covered in the text-only, common diseases section of the Resources chapter, but not to any great depth and, in most cases, in note form only. Miscellaneous diseases includes just 2 conditions: hyperthermia and aggression. Anesthesia is covered cursorily, but the difficulties encountered with anesthesia of lizards, which can be some of the trickiest of animals to immobilize satisfactorily, are not mentioned.

The quality of the color photographs is reasonable, the illustrations are simple but good. The quality of the overall production is marred by some careless spelling and editing, such as "biliverdan" and "bronchii." The quality of the color pictures in the reference section was poor on my system, and table formatting was often lost. No index or help program is included.

Compact disk technology is very suited to learning, if one has the ability to set aside a quiet time to work through the program, but I find that it is of limited use as a shelf reference, can be slow to access, and has limited portability. For the veterinarian or student who is looking for an introduction into one group of reptiles, *A Guide to the Lizards* provides a practical and enjoyable educational experience. However, no topic is covered in any depth, and other CDs will be needed for the other orders of reptiles: snakes, chelonians, and crocodilians. Presumably they will be forthcoming. The veterinarian who encounters the occasional lizard in practice, or wishes to develop expertise in the field of herpetology, would be better off purchasing a written text on reptile medicine.

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